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Name of Candidate: Sara Cohen Garson
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Thesis and Abstract Approved:



Committee Chairperson



Committee Member



Committee Member

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Sara Cohen Garson
Sara Cohen Garson
Department of Medical and
Clinical Psychology
Uniformed Services University
of the Health Sciences

Abstract

LIFE CHANGE AS A PREDICTOR OF CATECHOLAMINES, CORTISOL, ANXIETY AND
DEPRESSIVE SYMPTOMS

Sara Cohen Garson, Master's, 1994

Thesis directed by: Andrew S. Baum, Ph.D. and David S. Krantz,
Ph.D., Department of Medical and Clinical Psychology

Life change count and life change adjustment values were included in predictor models for urinary catecholamine levels, urinary cortisol levels, depressive symptoms and anxiety symptoms among motor vehicle accident survivors and minor injury control subjects. The ability of motor vehicle accident and minor injury exposure to duplicate aspects of the "toughened" neuroendocrine pattern induced in laboratory stress studies (greater catecholamine capacity and reactivity, and diminished cortisol responses) was assessed. Successive hierarchical multiple regressions were run to determine the predictive capacity of life change variables for hormone and symptom levels. Life change counts or adjustment ratings were effective predictors of depressive and anxiety symptoms at 6 months and 18 months following accident or injury. Few neurohormone associations with life change and mood scores were detected. However, some minor injury group associations and the neurohormone correlates of life counts proximate to accident/injury were consistent with some aspects of the "toughened" neuroendocrine pattern.

Life Change as a Predictor of Catecholamines, Cortisol,
Anxiety and Depressive Symptoms

Sara Cohen Garson
Master's Thesis
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Frequent reports of life changes preceding physical and mental illness have prompted numerous investigations of life change as a potential causal agent. Many studies have demonstrated a relationship between various aspects of life change and morbidity (Dohrenwend & Dohrenwend, 1981). Originally, change itself was considered to carry a high cost in physiological or health consequences. The work of Holmes and Rahe (1967) evaluated the amount of readjustment necessitated by recent life changes and detected a relationship with illness onset. Later studies have searched for more specific toxic aspects of change that could account for associations with morbidity. Negative and positive meaning (Sarason, Johnson & Siegel, 1978; Vinkour and Selzer, 1975), control (Dohrenwend & Dohrenwend, 1978) and appraisal and coping responses (Folkman, Lazarus, Gruen and Delongis, 1986) are among the attributes of life change that may help explain better or worse outcomes. The present study represents a departure from investigations of life change characteristics as predictors of outcomes. It examines life change as a possible moderator of neurohormone response patterns that may affect future life change experience and outcomes. This study's specific objective is to test hypotheses that levels of life change exposure represent individual differences that may affect adaptive ability.

It is widely accepted that stressful life changes, particularly losses, are associated with the onset of episodes of depressive disorder (Paykel, 1992). For the most part, investigation of life change as a factor in other health problems has produced less consistent associations. Unreliable methodology has been identified as a significant problem in this area of research. It is a complicated matter to examine phenomena dependent upon recall. Inaccurate memory may provoke a human inclination to search for or exaggerate past life changes to explain current hardship. While independent verification of reported life changes can limit some inaccuracies attributed to retrospective bias, verification is not always feasible. Furthermore, accurate description may not capture the content that matters. The potency of life change may not be determined by its characteristics alone. The personal meaning of a change may also drive the nature of physiological response. Characterizing the nature of response to life changes provides another approach to their evaluation. Newly established relationships between stress and consequent neuroendocrine shifts may turn out to be a useful way to monitor and clarify the impact of life changes on health.

Catecholamine and cortisol shifts reported in human and animal studies have stimulated a reconsideration of

stress impact on health. The altered neuroendocrine pattern revealed by these studies has led Richard Dienstbier (1992) to add a conceptual criticism to the early methodological criticisms of life change research. His conceptual objection is the assumption that stressful life changes generate exclusively negative health consequences. Dienstbier believes convergent results suggest that exposure to overwhelming stressors can be beneficial if exposure is brief and recovery time adequate. In animal and human studies, controlled stress exposure has been used to produce a pattern of neuroendocrine reactivity purported to increase stress stamina and emotional well-being. "Toughness" is the term Dienstbier uses to describe stress resilience produced in this manner.

Dienstbier's "toughness" theory turns upon the interplay of two types of arousal. SNS-adrenal-medullary arousal involves the hypothalamic stimulation of the SNS and adrenal medullae to generate the energy needed to confront acute stressors. A second type of arousal, pituitary-adrenal-cortical arousal, involves pituitary stimulation by the hypothalamus to activate cortisol release from the adrenal cortexes. Cortisol acts to sustain energy through the metabolism of stored fat and protein and also restrains inflammatory responses. Although cortisol release promotes survival during acute stress, elevated cortisol has also

been associated with negative effects such as anxiety (Lader, 1983) depression (Gold, Goodwin and Chrousos, 1988; Holsboer, 1992) and immunosuppression (Calabrese, Kling and Gold, 1987; Holsboer, 1992).

In "toughened" organisms, SNS-adrenal-medullary arousal appears to be enhanced and extended while adrenal-pituitary-cortical arousal appears to be delayed or avoided. Therefore, the benefits of sympathetic stimulation are fostered and the adverse effects associated with high levels of cortisol are limited. (The four specific neuroendocrine alterations that define this "toughened" pattern and will be described in detail later.) Manipulations such as intermittent shock, restraint, noise, aerobic exercise, handling, cold exposure and alternate species rearing have been used to induce "toughness" in animals. Weiss, Glazer, Pohorecky, Brick and Miller (1975) report two studies typical of animal "toughening" paradigms. In one study, the escape deficits of rats exposed to a single inescapable shock or cold swimming treatment were compared to escape deficits of rats exposed to repeated shock or cold swimming treatments. Unstressed rats served as controls. Prior to escape testing, animals in repeated treatment groups were exposed to the training stressor or a novel stressor (the alternate study stressor, either shock or cold swimming). Poorer escape performance was demonstrated by animals in the

single treatment groups. In the second study reported, central nervous system (cortical and hypothalamic) levels of norepinephrine and plasma cortisol were compared following shock. Control rats, rats previously exposed to repeated shock or cold swimming, and rats previously exposed to single shock were sacrificed after shock. Animals treated with single shock prior to sacrifice showed evidence of central norepinephrine depletion. Less reduction in central norepinephrine levels was found for those rats given repeated treatments prior to final shock exposure, particularly repeated shock treatments. A similar result was found for plasma cortisol levels. The greatest cortisol elevation was found for rats treated with a single shock. A much smaller elevation was found for rats treated with repeated shocks. However, attenuated plasma cortisol elevation was not found for the group treated with repeated cold swimming.

In humans, aerobic exercise has been tested as a "toughening" manipulation to increase stress resilience. Inconsistent results have been produced by studies that have evaluated catecholamine responses to mental stress for physically fit individuals and nonexercising individuals. However, Dienstbier, LaGuardia, Barnes, Tharp, and Schmidt (1987) have reported increased urinary catecholamines following mental stress in three controlled studies.

It is unlikely that controllable physical stress such as aerobic training is precisely comparable to the uncontrollable and threatening manipulations used in animal paradigms. Nor have the animal manipulations been found to be universally equivalent. Further, mental stressors can not be assumed to be equal to each other or equivalent to physical stressors. Nonetheless, several studies using different stressors have found sequential exposure to be associated with a similar neuroendocrine pattern and improved performance abilities.

This leads Dienstbier to suggest that there may be a physiological process of adaptation analogous to processes like learning or coping, and that this process may be stimulated by many types of demanding experiences (Dienstbier, 1992, 1989).

In his review of the literature, Dienstbier notes that "toughening" manipulations and the "toughened" neuroendocrine pattern have both been associated with positive performance abilities and personality attributes (Dienstbier, 1989, 1991, 1992). He suggests that the common element in the manipulations may be peripheral physiological arousal coupled with success, enhanced perceived control and adequate recovery time. Therefore, it follows that difficult but manageable life changes could "toughen". The question central to the current study is whether

intermittent life changes alter neuroendocrine parameters and increase capacity to withstand additional life changes.

There are four altered neuroendocrine capacities that characterize "toughness" (Dienstbier, 1991). First, an increased ability to maintain adequate central nervous system levels of catecholamine is described. Central nervous system norepinephrine depletion has been proposed as the mechanism for behavioral suppression demonstrated in learned helplessness paradigms. In humans, inadequate levels of central nervous system norepinephrine has been suggested as the etiology of some depressive disorders. Animal trials have demonstrated the ability of "toughening" to preserve central nervous system catecholamine levels. As reviewed earlier, Weiss, Glazer, Pohorecky, Brick, and Miller (1975) subjected rats to intermittent catecholamine-depleting stressors (inescapable shock, cold swimming) to reduce central norepinephrine depletion on subsequent stressor exposure. Hypothalamic and forebrain norepinephrine and tyrosine hydroxylase levels were higher in "toughened" animals and the behavioral suppression associated with norepinephrine depletion did not occur.

The second "toughness" capacity described reflects altered SNS-adrenal-medullary reactivity. "Toughened" organisms show lower levels of peripheral catecholamines at rest. However, exposed to severe stress, "toughened"

organisms show faster, stronger catecholamine responses that rapidly return to baseline levels. This response pattern permits more effort with less sustained arousal and increases endurance. Clearly physically adaptive, this capacity may have psychological advantages as well.

Dienstbier has found that aerobically trained subjects, challenged by psychological stressors (sound stress with performance task, Stroop test) showed a larger catecholamine response after their training and when compared to untrained control subjects (Dienstbier, LaGuardia, Barnes, Tharp, Schmidt, 1987). In rat stress exposure studies, there was evidence of a similar pattern in animals handled young. Lower baseline levels of adrenal tyrosine hydroxylase, higher adrenal tyrosine hydroxylase activity during stress exposure, and a more rapid return to baseline adrenal tyrosine hydroxylase levels were found (Pfeifer, 1976).

A third characteristic associated with "toughness" identified in aerobically trained animals and humans is increased sensitivity to peripheral catecholamines. Dienstbier reviews evidence that a fixed amount of infused catecholamine generates greater arousal in "toughened" animals and fit humans (Dienstbier, 1989, 1991, 1992). Increased sensitivity of beta-adrenergic receptors is postulated to account for enhanced arousal and lower resting catecholamine levels (Dienstbier, 1992).

The final altered capacity associated with "toughness" is delayed and curtailed pituitary-adrenal-cortical arousal. In rats handled as infants, stress-induced adrenal cortisol levels are lower and return to resting levels sooner than levels for rats not handled (Pfeifer, 1976; Hess, Denenberg, Zarrow, and Pfeifer, 1969).

These findings emphasize differences between "toughening" stress exposure and chronic, uncontrollable stress exposure. Chronic stress exposure has been associated with persistent physiological arousal under challenge conditions (Fleming, Baum, Davidson, Rectanus, and McArdle, 1987) and elevated resting levels of catecholamine and cortisol levels (Baum, Schaeffer, Lake, and Collins, 1986). Additionally, while the neuroendocrine pattern described by "toughness" has been associated with positive performance, affect, and immune status (Dienstbier, 1989, 1991, 1992), the neuroendocrine shifts associated with chronic stress appear detrimental. In most instances, task-induced catecholamine increases have been associated with improved performance. However, chronically elevated catecholamines have been associated with poorer psychological adjustment and more ailments (Baum, Schaeffer, Lake, Fleming, and Collins, 1986). Elevated cortisol has been associated with a host of negative outcomes, including poor performance, distress, defensiveness, depression,

anxiety and immunosuppression (Dienstbier, 1989, 1991)

Hypothalamic induction of SNS-adrenal-medullary arousal increases blood glucose to fuel both brain and muscle and may account for immediate performance gains found following stress manipulation. Moreover, adequate energy may have long-term effects as well as short-term effects. A history of acceptable stress outcomes may positively bias future secondary appraisals. Dienstbier proposes that "toughening" may foster challenge appraisal. By increasing perceived control, challenge appraisals may enhance SNS-adrenal-medullary arousal, limit pituitary-adrenal-cortical arousal and enhance the availability and perception of energy. Sustained energy is likely to improve performance and increase odds for success. Success may generate future positive appraisals. If stress exposures remain within the limits of capacity, a self-sustaining positive coping loop may be established that supports functioning and emotional well-being.

This line of thinking suggests that life change experience is a potential modifier of biological correlates to performance ability, anxiety, and depression. Therefore, life change experience could represent an alternative explanation for individual differences in trauma outcomes. More commonly, biological difference hypotheses to explain variability in stress response have been

constitutional in nature. For example, Chrousos and Gold (1992) have proposed constitutional stress system differences that set different stress vulnerability thresholds. Few biologically oriented theories of differential stress responses have addressed potential altering forces within stress exposure. Perceived control has been examined as a potential mechanism of stress effects. The present study considered life change characteristics as potential factors in stress outcomes.

Many efforts to examine stress-related psychopathology have relied on laboratory manipulations of animal models thought to mimic human experience (i.e., learned helplessness paradigms (Seligman, 1967), stress precipitation of depressive symptoms studies (Anisman, 1984), etc.). Dienstbier's model and evidence that peripheral catecholamine and cortisol levels are correlated with performance and affect, suggested that natural human experience and its neuroendocrine correlates could provide a viable design alternative. Two common human stressors, motor vehicle accidents and minor injuries, were selected as real life stress manipulations for the current study. Life change scores, urinary catecholamine levels, cortisol levels, anxiety symptoms, and depression symptoms were measured for survivors of life-threatening motor vehicle accidents and people who sustained minor injuries. The

ability to predict outcome variables from life change measures was assessed.

The possibility that life change contributes to "accident-proneness" has been addressed in previous investigations of motor vehicle accidents. Inconsistent findings have resulted (Selzer, Rogers and Kern, 1968, Selzer and Vinkour, 1974, Isherwood, Adam and Hornblow, 1982). The present study considered a different relationship. Rather than considering the correlation of prior life change to likelihood of accident exposure, the relationship of life change experience to responses to trauma was addressed. Accident exposure as a contributing factor to subsequent life change response was also investigated. Epinephrine, norepinephrine, cortisol levels and anxiety and depressive symptoms were evaluated as possible markers for stress vulnerability or resilience. Four hypotheses were tested.

The first hypothesis was that numbers of life changes prior to motor vehicle accident or minor injury would be correlated with levels of epinephrine, norepinephrine, cortisol, anxiety and depressive symptoms recorded one month after the accident. Specifically, more life changes prior to accident/injury would be associated with lower neurohormone levels, anxiety symptoms, and depressive symptoms. Mastery of prior life changes would be expected

to replicate processes generated by laboratory "toughening" manipulations and produce a "toughened" response pattern. Such findings would suggest prior stress survival as a mediator of rapid return to baseline neurohormone status and positive appraisal. No adjustment variable was available at visit 1, and no precise duration variables were measured, so adjustment ratings and recovery time could not be considered in the hypothesis.

The second and third hypotheses were related and were based on available, comparable life change counts and adjustment ratings for visits 3 and 5. A profile of low life change counts with high adjustment ratings was expected to be associated with lower levels of neurohormones and mood symptoms. This pattern of exposure would most closely approximate the "toughening" protocol of intermittent overwhelming stress exposure with recovery time. A profile of high life change counts with high adjustment ratings was expected to be associated with higher neurohormone levels and mood symptoms. Such a pattern would most closely approximate chronic stress exposure.

The final hypothesis was that life change counts and/or adjustment ratings at early time points would significantly predict neurohormone and mood symptom levels at later time points.

METHODS

Subjects

The sample for this study consisted of the first 124 subjects enrolled in a longitudinal study of motor vehicle accident survivors. Criteria for entry into the primary study limited participants to motor vehicle victims requiring shock trauma treatment. Subjects with severe head trauma or injuries whose conditions could not be stabilized within three weeks were excluded. Participants were accident victims who had endured a period of intense and threatening stress exposure. A control group was also included, made up of patients treated for minor injuries by the emergency room of the same hospital. Of the 124 participants, 94 were motor vehicle accident survivors and 30 were control group members.

Procedures

Subjects for the primary motor vehicle accident study were tested in their homes within 1 month post-accident/injury (visit 1), 3 months post-accident/injury (visit 2), 6 months post-accident/injury (visit 3), 12 months post-accident/injury (visit 4) and 18 months post-accident/injury (visit 5). Informed consent was obtained at visit 1. The same researcher made visits to collect data for each subject. Subjects were given verbal and written

instructions at each visit to promote proper questionnaire completion and specimen collection.

The research reported here is based on data collected at visits 1, 3, and 5 of the primary study. Life change data was derived from the Recent Life Change Questionnaire (Holmes and Rahe, 1967). Anxiety symptom and depression symptom scores were taken from the anxiety and depression subscales of the SCL-90R (Derogatis, 1977). Neuroendocrine values were determined by assay of fifteen-hour urine specimens (6pm to 9am) collected at each visit.

Measures

The Symptom Checklist 90R, is self-report inventory including 90 items that describe physical and emotional symptoms (Derogatis, 1977). Subjects are asked to rate the level of distress caused by each symptom over the course of the preceding week. Rating choices begin at 0 (Not At All Distressed) and increase to 4 (Extremely Distressed). A symptom reporting score may be computed from the total number of distressing symptoms experienced over the course of the week. More specific measures, distress severity scores, can be computed for each of nine subscales. These severity scores represent the average rating of the subscale items. Distress severity scores for the anxiety and depression subscales were included as variables in this study.

The Recent Life Changes Questionnaire (Holmes & Rahe, 1967) is a self-report measure that documents events characterized as health, work, home and family, personal or social, and financial changes occurring during a specified period of time. The designated time period is marked by consecutive 6 month intervals. Subjects are asked to evaluate the amount of adjustment necessitated by each endorsed change through the assignment of points (1-100). Total numbers of changes and total adjustment points are computed as separate scores to describe quantitative and qualitative aspects of stress exposure for that period of time.

In this study, the Recent Life Changes Questionnaire was completed at visit 3 (6 months post-accident/injury) to describe life changes occurring in the previous 2 years. At visit 5, the questionnaire was completed to describe life changes occurring the preceding year (a period covering 6 to 18 months post-accident/injury). Life change counts were tabulated for 6-month intervals throughout each specified time period. Although separate six month life change counts were computed, only two adjustment ratings, each spanning its complete time period, were produced. Consequently, the first adjustment rating covered life change demands experienced during the 18 months preceding the accident/injury until 6 months after the accident. The

second adjustment rating represented the life change demands experienced from 6 months post-accident/injury until 18 months post-accident/injury.

INSERT FIGURE 1 HERE

Life change counts used in the analyses were as follows. LCBAC, the number of endorsed changes for the 18 month period preceding the accident/injury, was the prior stress history variable. LCACC, the number of endorsed changes generated by the accident/injury and subsequent 6 months, was isolated for separate analysis. LCT3, the number of life changes endorsed at visit 3, totaled the life changes derived from stress history (LCBAC, 18 months), accident/injury exposure, and acute recovery (LCACC, 6 months). NEWLC, the number of endorsed changes for the 1 year period between visit 3 and visit 5, was computed to describe new life change experience.

For the purposes of these analyses, patterns of life change counts were presumed to suggest intermittency of stress exposures. Greater numbers of changes over equal time periods were presumed to reflect less available recovery time for any stress exposure. It would have been preferable to have collected data capturing the precise duration of each stress exposure.

Adjustment rating variables, presumed to reflect overall stress intensity for each specified time period, were defined in a similar way. CADJUST documented adjustment demands from the 18 months prior to the accident/injury until 6 months post-accident/injury (comparable to the life change count LCT3). EADJUST documented adjustment demands during the 1 year period between visits 3 and 5 (comparable to the life change count NEWLC).

Epinephrine, norepinephrine and cortisol values that constitute biological variables in the study were derived from 15-hour urine samples. This strategy permits assessment of SNS-adrenal-medullary system activity trends (as indicated by levels of free urinary epinephrine and norepinephrine) and pituitary-adrenal-cortical system activity trends (as indicated by cortisol levels). While these measures do not represent absolute levels of neurohormones or levels induced purely by stress exposure, shifts in these levels have been associated with arousal and appraisal choices. Because urine collection continues over several hours, the amount of hormone excreted is less likely to reflect the effects of a single acute stressor or quiescent period, and more likely to represent general arousal. A 24-hour collection would capture the effects of circadian surges and nadirs, and include more stress

exposures. However, many subjects can not comply reliably with a 24-hour urine collection. To counter the problems of this abbreviated collection time, all subjects were instructed to collect 15 hour specimens in the same manner and on the same schedule. Subjects maintained a diary during specimen collection documenting intake of substances that might influence their catecholamine levels (caffeine, tobacco, alcohol, foods and medications). Prior to freezing samples from the specimens, the urine was kept cool and preserved with sodium bisulfite.

Epinephrine, norepinephrine, and cortisol assays were performed in duplicate from frozen aliquots of the 15-hour specimens. In the assay, free catecholamines are converted to radio-labeled metabolites which are separated (thin layer chromatography) into dopamine, epinephrine, and norepinephrine metabolites. The radioactivity of the epinephrine and norepinephrine metabolite components of each duplicate is determined by scintillation counter and the counts are converted to concentration values.

Commercial radioimmunoassay kits are used to determine cortisol values (INCSTAR GAMMACOAT [¹²⁵I] Cortisol RAI Kit). The kits provide antibody coated tubes that bind cortisol. Cortisol contained in urine aliquots binds with the antibody as does an added fixed amount of radio-labeled cortisol. The more antibody that binds urinary cortisol,

the less antibody is available to bind radio-labeled cortisol. Ultimately, it is the labeled bound cortisol that is counted. Due to the reciprocal relationship of the amount of bound urinary cortisol to free cortisol, the radioactivity of the labeled cortisol can be used to calculate the concentration of urinary cortisol. Prior to data analysis, catecholamine and cortisol values were corrected for volume and converted to micrograms.

Results

Preliminary correlation analyses were run to determine if significant relationships between life change variables, catecholamines, cortisol, anxiety symptoms, and depressive symptoms could be detected in this sample. Potentially influential factors, group membership (motor vehicle accident or minor injury), gender, and age, were additional variables included in all analyses.

Several significant correlations were found for Visit 1 (1 month post accident/injury) variables. At this time, minor injury exposure was associated with higher life change counts (LCBAC) prior to injury ($r = .21, p < .04$). Additional analyses showed the mean life change count (LCBAC) for the minor injury group was 12.00 and the mean for the motor vehicle group was 8.71, $t(89) = -2.05, p < .05$.

ANOVA showed a main effect for LCBAC by group $F(1,90) = 3.99, p < .05$). Minor injury exposure was also associated with higher levels of epinephrine ($r = .27, p < .01$). The mean level of epinephrine was 9.75 mcg/ml for the minor injury group and 6.26 mcg/ml for the motor vehicle group, $t(35.16) = -2.51, p < .05$. In this sample, the control group may have had a significant stress history, an unexpected response bias, or greater epinephrine reactivity. However, across groups, a relationship between prior life change score and epinephrine was also found ($r = .25, p < .02$). Higher life change count (LCBAC) was associated with higher levels of epinephrine ($r = .25, p < .02$).

Gender and symptom associations were not surprising. The men participating in this accident study were younger than the women ($r = -.19, p < .04$); mean age men = 32.9 and mean age women = 37.8, $t(121) = 2.08, p < .05$). Women were more likely to report anxiety symptoms ($r = -.30, p < .01$) and depression symptoms ($r = -.32, p < .01$). Men were more likely to show higher levels of epinephrine ($r = .24, p < .01$) and cortisol ($r = .24; p < .01$), associations that may reflect gender differences and greater numbers of men (66) than women (57) in the sample at this visit. There was a strong positive association between reported anxiety symptoms and depression symptoms ($r = .78, p < .01$). Gender is not likely to account for the epinephrine difference in the minor

injury group. In both groups, gender distribution was similar, with slightly more males participating (Motor Vehicle Group: males = 49 and females = 44; Minor Injury Group: males = 17 and females = 13). Age was positively associated with norepinephrine ($r = .20, p < .03$). The mean age in this sample was 35. Associations among biochemical measures were small. As would be expected, epinephrine was highly correlated with norepinephrine ($r = .65, p < .01$). Its association with cortisol was smaller ($r = .36, p < .01$). A small positive relationship was detected between norepinephrine and cortisol ($r = .21, p < .03$) that could reflect the effects of on-going physical demands secondary to trauma.

Visit 3 data, collected at 6 months after accident/injury, showed similar correlations. Women remained more likely to report depression symptoms ($r = -.33, p < .01$) and anxiety symptoms ($r = -.28, p < .01$). LCT3, the life change count from 18 months preceding the accident/injury until 6 months after the accident/injury, was now found to be positively associated with reported depression symptoms ($r = .38, p < .01$) and reported anxiety symptoms ($r = .37, p < .01$). Epinephrine and norepinephrine remained correlated ($r = .53, p < .01$). Reported anxiety and depression scores also remained highly correlated ($r = .74, p < .01$). At visit 3, the first adjustment rating was

completed and CADJUST, an adjustment variable, was included in the analyses. CADJUST was related to reported depression ($r = .44$, $p < .01$) and reported anxiety ($r = .51$, $p < .01$). At the same time, the adjustment score was highly correlated with the life change count, LCT3 ($r = .70$, $p < .01$).

Additional age associations emerged at this visit. Younger participants were found to report higher life change counts ($r = -.28$, $p < .01$) and to estimate greater amounts of adjustment ($r = -.28$, $p < .01$).

At visit 5, 18 months after accident/injury exposure, many associations seen previously disappeared. In particular, gender associations (except for the fixed association with age) were lost. NEWLC, the life change count for the year between visit 3 and visit 5, was positively correlated with reported symptoms of depression ($r = .32$, $p < .02$) and anxiety ($r = .42$, $p < .01$). Epinephrine remained highly correlated with norepinephrine ($r = .70$, $p < .01$) and was also positively correlated with cortisol ($r = .28$, $p < .05$). Norepinephrine and cortisol were again associated ($r = .59$, $p < .01$). Reported anxiety symptoms and depression symptoms remained strongly, positively associated ($r = .83$, $p < .01$). EADJUST, the adjustment score for this time period, remained highly correlated with the life change score ($r = .81$, $p < .01$) and was also associated with reported anxiety ($r = .47$, $p < .01$) and with reported depression (r

=.38, $p<.01$).

A second series of correlations was run using the variable LCACC, a life change count that isolated life changes for the time of the accident/injury and the subsequent 6 months. LCACC was positively associated with LCBAC, the life change count for the 18 months prior to accident/injury ($r = .28$, $p<.01$) and LCT3, the life change count incorporating both LCBAC and LCACC ($r = .73$, $p<.01$). At visit 5, LCACC was associated with NEWLC, the life change count for the succeeding 12 months ($r = .54$, $p<.01$). The correlation of younger subjects with higher life change counts persisted regardless of life change interval (LCACC and age: $r = -.37$, $p<.01$; LCT3 and age $r = -.28$, $p<.01$). A similar pattern of anxiety associations was found. The correlation coefficient for LCT3 with anxiety was $r = .37$ at a significance level of $p<.01$ while the correlation coefficient for LCACC with anxiety was $r = .46$ at a significance level of $p<.01$. Depression symptom associations were almost identical for LCT3 and LCACC ($r = .38$, $p<.01$ and $r = .36$, $p<.01$, respectively. Adjustment rating (CADJUST) was associated with LCT3 ($r = .70$, $p<.01$) and LCACC ($r = .55$, $p<.01$). However, using this more acutely timed life change count (LCACC) revealed one unusual association at visit 3. Higher LCACC was associated with lower cortisol levels ($r = -.23$, $p<.05$). Visit 5 associations for LCACC varied

slightly from those found at visit 3. LCACC remained significantly associated with reported symptoms of anxiety ($r = .36$, $p < .01$), but its association with symptoms of depression was lost. LCACC was again found to be negatively associated with visit 5 cortisol levels ($r = -.31$, $p < .05$). In addition, LCACC was negatively associated with visit 5 norepinephrine levels ($r = -.30$, $p < .05$). Prior to regression analyses, correlations were run for reported amine-containing foods at visits with neurohormone, group, gender, and LCACC associations. No significant relationships were found between these variables and amine-containing food totals.

A model including group membership (motor vehicle accident or minor injury group), gender, age, and life change variables as predictors of neurohormone levels and mood symptoms was suggested by visit 1 correlations. This model was used to account for variance in epinephrine levels and self-reported anxiety and depression symptom levels at visit 1. There was not an adjustment variable comparable to the visit 1 life change count variable (LCBAC). However, visit 3 and visit 5 adjustment correlations supported the inclusion of adjustment scores in the predictor model whenever possible. Neurohormone values were only included as criterion variables when significant correlations with life change or adjustment variables had been found.

Hierarchical multiple regression was used to determine the contribution of each predictor variable to account for variance in each criterion variable. At visits 3 and 5, the model included previously measured predictor values that could be expected to influence later values. Because life change count variables had been highly correlated with adjustment scores, each was entered as alternate last steps in separate regressions. Because life change and adjustment were too highly correlated to be considered independent variables, interaction analyses were not done.

The model proved to be a useful predictor of epinephrine, self-reported anxiety symptoms and depression at visit 1. Nineteen percent of the variance in epinephrine levels was accounted for by the total model. Group accounted for 8% of the variance (Minor injury was associated with higher levels of epinephrine). Gender accounted for an additional 6% (Males had higher levels of epinephrine). Age added little, but the life events score (LCBAC) accounted for an additional 5% of the variance (Higher life change count was associated with higher levels of epinephrine).

INSERT TABLE 1 HERE

Sixteen percent of the variance in reported

depression score was accounted for by the model at visit 1. However, gender was the only significant predictor and accounted for 14% of that variance (Females reported more depressive symptoms).

INSERT TABLE 2 HERE

Twelve percent of the variance in reported anxiety score was accounted for by the model. Again, gender accounted for most of the variance in anxiety symptoms (9%) identified by the model (Females reported more anxiety symptoms). No other predictors accounted for significant amounts of variance in reported anxiety.

INSERT TABLE 3 HERE

The model, using either life change counts or adjustment ratings as final predictor entered, was tested again with visit 3 and visit 5 data. Criterion variables (anxiety symptoms, depression symptoms, cortisol levels, or norepinephrine levels) were limited to those significantly correlated with predictor variables at visit 3 or visit 5 .

For visit 3 and visit 5 analyses, the model was tested with two life change count configurations. One configuration used the life change count for the total 2

year period prior to accident/injury as a predictor variable. The other configuration split the total life change count to allow the 6 month count including the accident/injury to be used as a separate predictor variable.

In the first configuration, LCBAC, the life change count for 18 months prior to accident/injury was entered as a separate step prior to LCACC, the acute accident-related life change count.

Three regressions were run with the criterion variables anxiety symptom score, depression symptom score and cortisol level. The model accounted for 27% of the variance in anxiety symptom score with gender accounting for 8% of the variance (Females reported more anxiety symptoms) and LCACC accounting for 14% of the variance (Higher life change count was associated with more reported anxiety symptoms). Twenty-six percent of the depression symptom score variance was accounted for by the model with gender accounting for 11%, LCBAC (the life change count for the 18 months prior to accident/injury) accounting for 6%, and LCACC (the acute accident-related life change count) accounting for 7% of the variance. Again, female gender was associated with more reported depressive symptoms and higher life change counts were associated with more reported depressive symptoms. Although LCACC had been significantly

correlated with cortisol levels, no predictive ability was apparent when LCACC was included in this model.

INSERT TABLE 4 HERE

In the second configuration, LCT3, the life change count that combines LCBAC and LCACC, was the final life change count predictor entered. This configuration permits consideration of the relative predictive contribution of adjustment, since an adjustment score is calculated for the life change experienced during this total time period. Therefore, a comparable model was tested using CADJUST, the adjustment rating that parallels LCT3, as the final predictor variable.

Significant predictors of anxiety and depression scores were gender (Women were more likely to report symptoms of depression) and LCT3 or CADJUST. LCT3 accounted for 7% of the variance in symptoms of depression and 11% of the variance in anxiety symptoms. Substitution of the adjustment score for the life change count accounted for slightly more variance in depression symptoms (9%) and anxiety symptoms (15%). (In all instances, the higher the life change variable score, the higher the negative mood score.) This finding could suggest that personal meaning may carry its own impact, separate from amount of stress

exposure, although about the same amounts of variance was accounted for by the simple change counts and adjustment and counts were highly correlated.

INSERT TABLE 5 HERE

For visit 5 analyses, the model was again tested with two life change count configurations. In the first configuration, LCBAC (the life change count for 18 months prior to accident/injury) was entered first, followed by entry of LCACC (the acute accident-related life change count) and as the final step, NEWLC (the life change count for the year between visits 3 and 5) was entered.

Three regressions were run with the criterion variables anxiety symptom score, norepinephrine level and cortisol level.

The overall model lost some predictive ability at visit 5. The model no longer predicted depression symptom score variance. Twenty-nine percent of the variance in anxiety symptom score was explained with 14% accounted for by LCACC and 11% accounted for by NEWLC. (Higher life change counts were associated with higher anxiety symptom scores.) The negative correlation of LCACC and norepinephrine was not apparent in this model. Embedded in an otherwise non-significant model, LCACC accounted significantly for 11% of

the variance in cortisol level. In this instance, a negative relationship was found; higher life change counts associated with lower levels of cortisol.

INSERT TABLE 6 HERE

In the second configuration of the visit 5 predictor model, LCT3 (the life change count that combines LCBAC and LCACC counts) was entered prior to NEWLC (the most recent life change count). A comparable model was tested with CADJUST (the adjustment rating that parallels LCT3) and EADJUST, (the adjustment rating that parallels NEWLC) entered as the last two predictor variables.

Overall, the model using LCT3 and NEWLC as life change count variables accounted for slightly less variance in anxiety symptom score (25%) than the model that split LCT3 into pre-accident and post-accident life change counts (29%). However, this configuration accounted for 21% of the variance in depression symptom score, variance which could not be explained using the first configuration. The adjustment rating at visit 5 (EADJUST) was the final and only significant element in the adjustment-oriented model, but accounted for greater amounts of depression and anxiety symptom score variance than had NEWLC (the comparable life

change count). EADJUST could explain 23% of the anxiety symptom score variance and 13% of the depression score variance. (Life change variables were positively related to mood symptom scores.) From visit 1 to visit 5, predictive abilities of the life change count and adjustment variables increased coinciding with decreased predictive ability for gender.

INSERT TABLE 7 HERE

Correlations in this data support a model including exposure type, gender, age, and life change characteristics to predict reported anxiety and depression symptoms. However, correlations do not determine the causal direction of the variables' relationships. No significant correlations were found linking reported depressive symptoms with cortisol levels. This eliminated the possibility of testing depression-induced cortisol levels as predictors of adjustment appraisal. However, there were visit 3 and visit 5 correlations linking depression or anxiety symptoms with life change and adjustment scores. These findings highlighted the possibility that depression or anxiety might be influencing the experience of life changes, recall of life changes, or appraisal of adjustment demands.

This causal direction is also consistent with the

"toughness" model. . Dienstbier recognizes that on-going depression or anxiety could drive persistent arousal to transform an acute intermittent stress exposure to a chronic, catecholamine-depleting, cortisol-elevating experience. To consider this possibility, alternative models were tested at visit 3 and visit 5. Depression and anxiety scores were entered as predictor variables in the alternative models to attempt to account for variance in life change counts and adjustment ratings.

At visit 3, the original model accounted for slightly more variance than the alternative models. Life change score accounted for slightly more variance in depression symptoms and anxiety symptoms than mood symptoms accounted for life change variance. More specifically, LCT3 (life change count for the 18 months prior to accident/injury and 6 months after accident/injury) accounted for 7% of variance in depression scores and 11% of the variance in anxiety scores. Using the alternative models, 4% of the variance in LCT3 scores could be explained by the depression scores and 10% by the anxiety scores.

However, there was little difference between the ability of adjustment ratings to explain depression and anxiety score variance and the ability of depression or anxiety scores to explain adjustment rating variance. CADJUST accounted for 9% of the variance in the depression

scores and 15% of the variance in the anxiety scores. Using the alternative models, 8% of CADJUST variance could be explained by depression scores, while 14% could be explained by anxiety scores.

When LCACC (the acute accident-related life count) was the criterion variable, one alternative model reached significance. That model included anxiety as a predictor. Once again there was little difference between ability to predict life change variance from anxiety and the ability to predict anxiety variance from life change count. Specifically, anxiety symptom scores from visit 1 and 3, accounted for 15% of the variance in LCACC, while LCACC accounted for 14% of the variance in anxiety symptom scores. (Results not tabled).

Alternate models addressing visit 5 adjustment performed similarly to visit 3 models. EADJUST (adjustment rating for life changes during the year between visit 3 and visit 5) accounted for 13% of the variance in depression scores and 23% of the variance in anxiety scores. Using the alternative models, 11% of EADJUST variance could be explained by depression scores and 22% by anxiety scores.

However, there were some differences when the visit 5 life change count was analyzed. NEWLC accounted for 7% of the variance in depression scores and 14% of the variance in anxiety scores. Using the alternative models, depression

scores accounted for 21% of variance in NEWLC and anxiety scores accounted for 22% of NEWLC variance. In all instances, associations between mood symptom scores and life change counts were positive.

INSERT TABLE 8 AND TABLE 9 HERE

One final series of regressions was done. Life change counts and adjustment ratings were highly correlated, but appeared to vary in predictive ability for anxiety and depression symptom variance. Hierarchical regressions including both life change counts and adjustment ratings were run at visit 3 and visit 5 with anxiety and depression symptoms as criterion variables. Life change counts and adjustment ratings were entered as second to last and last steps in the regressions. The regressions were run twice to permit the order for the last two steps to be alternated. In each instance, the increment of unique variance accounted for by the last step variable was tested for significance.

At visit 3, models with CADJUST as the final predictor variable, had significant increments in explained variance of depression and anxiety scores ($F(1,79) = 4.39, p < .05$; and $F(1,79) = 10.16, p < .01$, respectively). Models with life change counts as last predictor variables did not show significant increments in explained variance of

depression and anxiety scores. At visit 3, adjustment was a more effective predictor.

However, at visit 5, none of the model configurations showed significant increments in explained variance after entry of final predictors. This may reflect the effects of a smaller N (49) and additional predictors (repeat measures) at visit 5. The limited N available at visit 5 reflected subject loss more than missing data points. Nothing can be determined about the relative predictive abilities of life change count and adjustment at visit 5.

Discussion

This study examined the possibility that life change history influenced catecholamine, cortisol, anxiety and depression characteristics following exposure to motor vehicle accident or minor injury. Neurohormone levels and mood symptoms were investigated as markers of previous life change. Life change history, expressed in simple counts or overall adjustment ratings was evaluated as a supplemental predictor of neurohormone or mood states following new life change exposure. Tenets of Dienstbier's "toughness" theory were used to develop specific hypotheses consistent with the research questions.

Correlations for visit 1 variables were dominated by gender associations and group membership findings. Prior life change count and epinephrine level were found to be positively associated with minor injury group membership. At visit 3, modest correlations among the hormone, anxiety and depressive symptom measures and life change counts and adjustment ratings were found. Few associations were detected in the visit 5 data. However, correlations of life change counts and adjustment ratings with anxiety and depressive symptoms persisted. When a circumscribed accident-focused life change count was isolated (LCACC), three hormonal associations emerged. LCACC was negatively correlated with cortisol level at visit 3 and negatively correlated with norepinephrine and cortisol levels at visit 5. However, these neurohormone correlations were small and significant at the .05 level.

Hierarchical multiple regression was done to describe variance in neurohormone levels and mood symptoms that could be explained by group, gender, age or life change variables. Life change variables emerged as effective predictors at visit 3, with higher life change scores associated with more reported mood symptoms. The accident-focused life change count (LCACC) explained more variance in anxiety symptoms than gender and the more inclusive life change count (LCT3) explained greater amounts of variance in

depression than gender. At visit 5, life change variables remained predictors of anxiety and depression symptoms. Adjustment ratings were more effective predictors for mood symptom variance than life change counts at visit 3 only.

Life change variables were not necessarily better predictors of mood symptoms than mood symptoms were predictors of life change variables.

The first hypothesis, that more historical life changes would be correlated with lower neurohormone levels and fewer visit 1 anxiety and depression symptoms was not confirmed. There were no associations between prior life change count and anxiety or depressive symptoms. The positive association of life change count and epinephrine level does not suggest the "toughness" reactivity pattern of increased catecholamine arousal with rapid return to baseline. However, coupled with the correlation of minor injury group membership with higher life change counts and epinephrine levels this association could suggest the effects of chronic stress on arousal and appraisal. More precise duration measures to establish the chronic or intermittent nature of prior life changes could clarify these findings. In addition, appraisal choices as outcomes or precipitants would need to be investigated to fully consider these associations. Finally, without a precise stress history for the period immediately preceding and

including the collection of urine, it is possible that they reflect other than resting values.

Life change count variables (LCT3, NEWLC) and life change adjustment variables (CADJUST, EADJUST) were too highly correlated to be analyzed as independent and potentially interactive variables (visit 3: $r = .70$, $p < .01$; visit 5: $r = .81$, $p < .01$). Neurohormone associations found involved life change counts without comparable adjustment ratings (LCBAC and LCACC). Therefore the interaction hypotheses linking life change counts and adjustment ratings with neurohormone and mood symptom levels, could not be evaluated. However, it was interesting that the neurohormone associations with LCACC, did parallel in part "toughness" neurohormone patterns. The greater the LCACC (life change count proximate to the accident/injury), the lower the cortisol level was at visit 3 ($r = -.23$, $p < .05$). and the lower the cortisol and norepinephrine levels were at visit 5 ($r = -.31$, $p < .05$ and $r = -.30$, $p < .05$, respectively). These findings would be consistent with lower resting catecholamines and reduced cortisol reactivity that could be produced by "toughening".

The final hypothesis was that life change counts and/or adjustment ratings at early time points could significantly predict neurohormone and mood symptom levels at later time points. Scattered significant predictors in

visit 3 and visit 5 regressions offered some support for this hypothesis. It is possible that the predictive ability of concomitant adjustment ratings for mood variance, shown to be superior to life change counts at visit 3, actually reflects the effects of recovery from major trauma. As recovery demands diminish, other life change demands may gain importance. Daily hassle severity ratings at each time point could support or disconfirm this possibility.

Clearly, this study did not find much evidence that motor vehicle accidents or minor injuries operated as "toughening" stress exposures for this sample. However, the data confirm the importance of investigating personal meaning and appraisals as mediators of trauma responses. Gender, a significant predictor accounting for anxiety and depression levels at visit 1, was no longer predictive at visit 5. It would have been useful to examine feelings of vulnerability, or loss of control experienced by subjects in this study. It is possible that vulnerability or control concerns lingered for traumatized women.

Minor injury group differences could reflect mediating effects of learning and appraisal on recall. Minor injury controls reported higher life change scores prior to injury. Exposure to a life-threatening trauma, as experienced by motor vehicle accident survivors, may recalibrate personal definitions for stressful life changes.

The motor vehicle accident survivors may have minimized the importance of other life changes to the point of not reporting them or even forgetting them. Less traumatized minor injury group members may have recorded more life changes because they have attended to more life changes or judged more changes to be meaningful. Less experience evaluating potential harm and testing survival capacity may serve to direct attention to changes that could be safely disregarded. It is also possible that in the context of many life changes, minor accidents are more likely to occur.

Correlations of neurohormones across time revealed little. While epinephrine and norepinephrine values were significantly and positively correlated with their prior values, cortisol values were not. Nor were consistent correlations between neurohormones found, although epinephrine and norepinephrine were frequently associated within visits, and norepinephrine and cortisol were sometimes associated within visits. Neurohormone levels measured during stress exposure, or in patient samples, might show consistent informative shifts that were not found in this study.

In conclusion, the neurohormone findings needed to support most of the hypotheses generated by the "toughness" model were not found in this study. Due to the large number of analyses, there is also the possibility of Type 1 error.

Further study would be benefited by fewer hypotheses, concomitant coping and mastery indices, and more precise measurement intervals. Immediate measurements under more severe circumstances, a difficult paradigm to operationalize with naturally occurring stressors, might yield more supportive findings. Nonetheless, these findings suggest life change assessment as an important component in predictive models for depressive and anxiety symptoms following accident/injury. These findings and the comparative ease of life change assessment suggest that life change assessment may be a practical screening strategy to identify those experiencing anxiety or depressive symptoms, or at risk for such symptoms, following accident/injury exposure.

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Table 1

Predictor Model for Epinephrine at Visit 1

Variable	RSQ	F (EQN)	SIG F	RSQCH	F CH	SIG CH
Group	.08	7.08	.009	.08	7.08	.009
Gender	.14	6.83	.002	.06	6.16	.015
Age	.15	4.77	.004	.01	.70	.406
LCBAC	.19	4.90	.001	.05	4.65	.034

LCBAC = Life change count 18 months before the
accident/injury

Table 2

Predictor Model for Depressive Symptoms at Visit 1

Variable	RSQ	F (EQN)	SIG F	RSQCH	F CH	SIG CH
Group	.00	.22	.641	.00	.22	.641
Gender	.14	7.13	.001	.14	14.01	.000
Age	.14	4.70	.004	.00	.00	.970
LCBAC	.16	3.97	.005	.02	1.66	.202

LCBAC = Life change count 18 months before the accident/injury

Table 3

Predictor Model for Anxiety Symptoms at Visit 1

Variable	RSQ	F (EQN)	SIG F	RSQCH	F CH	SIG CH
Group	.02	1.55	.217	.02	1.55	.217
Gender	.11	5.49	.006	.09	9.28	.003
Age	.11	3.73	.014	.00	.30	.548
LCBAC	.12	2.82	.030	.00	.21	.651

LCBAC = Life change count 18 months before the accident/injury

Table 4

Visit 3 Variance Accounted For (Rsquare Change)

Variable	ANX SYM	DEP SYM	CORTISOL
Group	NS	NS	NS
Gender	.08**	.11**	NS
Age	NS	NS	NS
LCBAC	NS	.06*	NS
LCACC	.14**	.07**	NS
TOT MODEL	.27**	.26**	NS

LCBAC = Life change count 18 months before the accident/injury

LCACC = Life change count associated with accident/injury and subsequent 6 months

* $p < .05$ ** $p < .01$

Table 5

Visit 3 Variance Accounted For (Rsquare Change)

Variable	ANX SYM	DEP SYM	Variable	ANX SYM	DEP SYM
Group	NS	NS	Type	NS	NS
Gender	NS	.04*	Gender	NS	.05*
Age	NS	NS	Age	NS	NS
LCT3	.11**	.07**	CADJUST	.15**	.09**
TOT MODEL	.13**	.11**	TOT MODEL	.17**	.14**

LCT3 = Life Change count for 18 months prior to
accident/injury plus 6 months after accident/injury.

CADJUST = Adjustment Score for same time period.

* $p < .05$ ** $p < .01$

Table 6

Visit 5 Variance Accounted For (Rsquare Change)

Variable	ANX SYM	NOREPI	CORTISOL
Group	NS	NS	NS
Gender	NS	NS	NS
Age	NS	NS	NS
LCBAC	NS	NS	NS
LCACC	.14**	NS	.11*
NEWLC	.11*	NS	NS
TOT MODEL	.29*	NS	NS

LCBAC = Life change count before the accident/injury.

LCACC = Life change count associated with accident/injury
and subsequent 6 months

NEWLC = Life Change count for 12 months between visit 3 and
visit 5.

* $p < .05$ ** $p < .01$

Table 7

Visit 5 Variance Accounted For (Rsquare Change)

Variable	ANX SYM	DEP SYM	Variable	ANX SYM	DEP SYM
Group	NS	NS	Type	NS	NS
Gender	NS	NS	Gender	NS	NS
Age	NS	NS	Age	NS	NS
LCT3	NS	.09*	CADJUST	NS	NS
NEWLC	.14**	.07*	EADJUST	.23**	.13**
TOT MODEL	.25*	.21*	TOT MODEL	.31**	.26*

LCT3 = Life Change count for 18 months prior to
accident/injury plus 6 months after accident/injury.

NEWLC = Life Change count for 12 months between visit 3 and
visit 5.

CADJUST = Adjustment Score for same time period as LCT3.

EADJUST = Adjustment Score for same time period as NEWLC.

* $p < .05$ ** $p < .01$

Table 8

Alternative Model with Depression Score Predictor

Visit 3 Variance Accounted For (Rsquare Change)			Visit 5 Variance Accounted For (Rsquare Change)		
Variable	LCT3	CADJUST	Variable	NEWLC	EADJUST
Group	NS	NS	Type	NS	.08*
Gender	NS	NS	Gender	NS	NS
Age	.10**	.08**	Age	NS	NS
Dep Sym	.04*	.08**	Dep Symp	.21**	.11*

LCT3 = Life Change count for 18 months prior to accident/injury plus 6 months after accident/injury.

NEWLC = Life Change count for 12 months between visit 3 and visit 5.

CADJUST = Adjustment Score for same time period as LCT3.

EADJUST = Adjustment Score for same time period as NEWLC.

* $p < .05$ ** $p < .01$

(Variance Accounted For in the Table 8 model represents the sum of unique variance accounted for when repeated measures were included in the regressions. The most conservative level of significance is reported.)

Table 9

Alternative Model with Anxiety Score Predictor

Visit 3 Variance Accounted For (Rsquare Change)			Visit 5 Variance Accounted For (Rsquare Change)		
Variable	LCT3	CADJUST	Variable	NEWLC	EADJUST
Group	NS	NS	Type	NS	.08*
Gender	NS	NS	Gender	NS	NS
Age	.10**	.08**	Age	NS	NS
Anx Symp	.10*	.14**	Anx Symp	.22**	.22*

LCT3 = Life Change count for 18 months prior to
accident/injury plus 6 months after accident/injury.

NEWLC = Life Change count for 12 months between visit 3 and
visit 5.

CADJUST = Adjustment Score for same time period as LCT3.

EADJUST = Adjustment Score for same time period as NEWLC.

* $p < .05$ ** $p < .01$

(Variance Accounted For in the Table 9 model represents the
sum of unique variance accounted for when repeated measures
were included in the regressions. The most conservative
level of significance is reported.)